REMARKS

The application has been amended. Claims 43 and 47 have been amended, claims 1-27 have been canceled and claims 51-71 have been added. Please charge the additional claim fees in the amount of $282.00 to our deposit account 08-2461. Reconsideration of the application is respectfully requested.

In the Preliminary Amendment, Applicants attempted to cancel original claims 11-27 of the grandparent application (Serial No. 08/811,473), and amend claims 1-10 of the grandparent. However, in the Office Action mailed 2/27/02, the Examiner alleges that claims 1-27 of the grandparent are not in the present case.

Applicants believe that original claims 1-27 of the grandparent application should have been retained in the present application, because they were not expressly canceled at the time of filing the present case. However, to assist the Examiner, Applicants now request that claims 1-27 be canceled without prejudice to the extent that Applicants believe they were retained in this case. Claims 28-50, which have been accepted by the Examiner for examination purposes, remain in the case numbered as such, with any new claims being numbered from claim 51.

Original claims 1-10 of the grandparent are now present as new claims 53-62. It is noted that new claims 53, and 58-62 correspond substantially to the original claims, but have been amended.

The Examiner has rejected claims 28-50 under the doctrine of obviousness-type double patenting "as being unpatentable over claims 1-10 of U.S. Patent No. 601167". Applicants believe that the Examiner has cited an incorrect patent number, and that the Examiner likely intended to cite U.S. Patent No. 6,001,067 instead. To the extent that Applicants are correct in this regard, upon receipt of a notice of allowance, Applicants will file a terminal disclaimer as

permitted under 35 U.S.C. §253 in order to obviate the double patenting rejection of claims 28-50.

The Examiner has further rejected claims 43, and 48-50 under 35 U.S.C. §102 (e) as being anticipated by U.S. Patent No. 5,791,344 to Schulman et al.(henceforth referred to as Schulman). The Examiner states the following:

> **Schulman et al discloses a device including a housing 80 for being implanted in a host, a means, including a membrane with glucose oxidase and the electrodes mounted thereon to measure glucose concentration, and a bioprotective membrane 100 that is substantially impermeable to macrophages.**

Applicants respectfully traverse the rejection under §102 (e) on the grounds that (1) Schulman, et al. fails to teach or disclose, *inter alia*, a housing of size and configuration for wholly implanting the device as provided by the present invention; and (2) Schulman fails to teach or provide an enabling disclosure of "continuous glucose sensing". These points will now be addressed in further detail below.

Schulman discloses a patient monitoring system for measuring a substance in a biological fluid or tissue. The Schulman monitoring system includes an enzymatic sensor adapted to be inserted into a host that is connected *via* a cable to a monitor located outside the patient's body. For example, as stated in column 2, lines 60-62 of Schulman, 'The electrical signals generated by the sensor ("sensor signals") are delivered through a suitable interconnect cable to a monitor.' Moreover, in column 6, lines 36-38 of Schulman it states: "The sensor assembly 32 is electrically connected to the glucose monitor by means of an interconnect cable 40." Furthermore, Schulman states in column 4, lines 35 and 36 that the sensor is coupled to an external monitor through a connector and two- or three-conductor cable. Thus, in contrast to the present invention, as, for example, recited in amended claim 43, the Schulman device is not wholly implantable in that the patient needs to remain electrically connected to an external monitor in order to continue to receive information from the device. Because of the well-known risk of

serious infection, such a device is primarily useful for bedside monitoring of the patient. For example, in column 4, lines 6-8 of Schulman, it states the following: "Such system is particularly suited for use in a hospital environment or other in-patient setting."

Furthermore, Schulman fails to disclose a sensing device capable of continuous glucose sensing as set forth in amended claim 43, for example. On page 9, lines 20-25, of Applicants' specification, it states "The phrase 'continuous glucose sensing' refers to the period in which monitoring of plasma glucose concentration is continuously carried out. More specifically, at the beginning of the period in which continuous glucose sensing is effected, the background sensor output noise disappears, and the sensor output stabilizes (e.g., over several days) to a long-term level reflecting adequate microcirculatory delivery of glucose and oxygen to the tip of the sensor." Furthermore, on page 10, lines 1-2 of Applicants' specification, it states "Failure of adequate vascularization or consistent contact of tissue with sensor will result in failure of continuous glucose sensing." Independent claims 43, 63 and 69 all, for example, call for a device which is capable of continuous glucose sensing, none of which are or can be anticipated by Schulman.

The present invention describes a wholly implantable device suitable for long-term continuous glucose sensing as defined in Applicants' specification. In particular, the present inventors have recognized that Foreign Body Capsule (FBC) formation is the dominant event surrounding long term implantation of any sensor and that the formation must be enhanced to support sensor performance. The unique architecture of the device of the present invention allows for there to be a dependable flow of blood to deliver glucose to the implanted device at a concentration representative of that in the vasculature. This is accomplished *via* an angiogenic layer that serves to promote vascularization in the sensor interface region and fixate the sensor tip in the tissue as, for example, now set forth in claims 66 and 69.

Moreover, the devices of the present invention become secured with the tissue of the subject by means of a capsular attachment layer, thereby reducing or eliminating "motion

artifact", which contributes to unreliable results. This is accomplished by using materials, such as surgical-grade polyester velour that encourage Foreign Body Capsule tissue to aggressively grow into the materials and form a strong mechanical bond. This fixation of the implant in its capsule is essential to prevent "motion artifact" which contributes to unreliable results. The non-smooth surface of the capsular attachment layer 16 is shown in Figure 1B of Applicants' specification.

In contrast to the present invention, the Schulman device is a smooth surface device that, if implanted subcutaneously, would evoke a classical foreign body capsule, such that long-term availability of glucose to the sensor would be blocked. In particular, outer sheath 100, which is in contact with the tissue, is disclosed as being silicone rubber, which as commonly known in the art would be smooth in texture. Schulman neither teaches nor discloses modifying the silicone sheath so as to prevent the formation of a glucose impermeable barrier during long-term implantation. Moreover, Schulman neither discloses nor suggests the use of an angiogenic layer, as particularly recited in claim 53, to promote the microcirculatory delivery of glucose and oxygen to the sensor tip, which is necessary for continuous glucose sensing as defined in Applicants' specification. Furthermore, the Schulman device does not include a capsular attachment layer or any other securing means, and as such would be susceptible to "motion artifact", which as described above and in Applicants' specification would contribute to unreliable results. Thus, this device would not be useful for continuous long-term monitoring of glucose.

The Examiner has further rejected claims 44 and 45 under 35 U.S.C. §103(a) as being unpatentable over U.S. patent No. 5,791,344 to Schulman, et al. The Examiner is of the opinion that the exact pore size and the exact membrane material would have been obvious to one skilled in the art. Since dependent claims 44 and 45 include all the limitations of patentable independent claim 43, Applicants submit that they are also patentable over the Schulman reference.

Applicants acknowledge the allowability of claims 46 and 47 and thank the Examiner for same. Claim 47 has been corrected to depend from claim 46.

Applicants submit that new claims 51-71 are being presented to further define the invention.

Having responded in full to the present Office Action, it is respectfully submitted that the application is in condition for allowance. Favorable action thereon is respectfully solicited.

Pursuant to §1.56, attached hereto is form PTO-1449 identifying additional references which have come to the attention of the undersigned. Since these references are being submitted after receipt of a first Office Action under §1.97 (c), please charge the required fee of $180.00 to our Deposit Account No. 08-2461.

Should the Examiner have any questions, the Examiner is invited to call the undersigned at the telephone number listed below.

Respectfully submitted,

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